REMARKS

Claims 13-26 are pending in this application.

The Examiner stated that the substitute specification filed on January 4, 2002 has not been entered because no marked-up copy was provided and that no declaration with respect to the substitute specification containing new matter was made. According to Applicant's records, a marked-up copy indicating the changes made to the original specification was submitted along with the substitute specification. Applicant respectfully requests that the Examiner review the files to see if it can be located. If the Examiner cannot locate the marked-up copy, Applicant requests her to contact the Applicant at the number indicated below so that the marked-up copy can be provided expeditiously to the Examiner.

Applicant hereby declares that the substitute specification filed on January 4, 2002 contains no new matter. Accordingly, acceptance of the substitute specification is respectfully requested.

All amendments to the specification submitted herein assumes that the substitute specification has been accepted by the Examiner.

The Examiner objected to the specification as failing to provide proper antecedent basis for the claimed subject matter. Specifically, the Examiner stated that the language of the claims are not disclosed in the specification. In response, Applicant has incorporated all of the claim language into the Summary of the Invention portion of the substitute specification. No new matter is added because the claims are considered to be a part of the application.

The Examiner objected to the Abstract because the clause "by o different analysis processes" is inconsistent with the specification. Applicant is hereby submitting a replacement Abstract with a replacement clause of "by τ different analysis processes" for consistency.

The Examiner objected to the specification/drawings because description of figures refer to subparts in the figures that are not present. Applicant respectfully submits that while the original specification does have the errors, the substitute specification contains

corrections of those errors. Applicant again requests acceptance of the substitute specification.

The Examiner rejected claims 13-24 under 35 U.S.C. Section 112, first paragraph, as failing to comply with the written description requirement. The Examiner stated that the phrase "determining said liquid ratio quantitatively" does not have support in the specification. That phrase is an error and Applicant has amended the claim to recite "liquid fractions" rather than "liquid ratio". The phrase has support in original claim 1 and in the Summary of the Invention portion of the specification.

The Examiner rejected claims 13-24 under 35 U.S.C. Section 112, second paragraph, as being indefinite. For claim 13, the Examiner stated that "said liquid ratio" has no support in the specification. As discussed above, Applicant has amended that phrase to "said liquid fractions". The Examiner also stated that "in a subsequent separating steps" appears to have an error. Applicant thanks the Examiner for pointing out the error. That phrase has been changed to recite "in a subsequent separating step".

For claim 14, the Examiner stated that certain phrases are confusing. Applicant has amended claim 14 to make it clearer.

For claim 16, the Examiner stated that "selected as quantification methods" is unclear. Applicant has amended the phrase to refer to the quantification processes of line 12 of claim 13.

For claim 19, the Examiner stated that "selected as quantification methods" is unclear. Applicant has amended the phrase to refer to the quantification processes of line 12 of claim 13.

For claims 20-21, the Examiner asked whether "preferably in the n*96 grid ..." is a limitation. Applicant has deleted the phrase in the claims and added new dependent claims 25-26 with the same phrase.

For claim 23, Applicant has deleted the phrase "which are known per se" to avoid any confusion.

For claim 24, Applicant has clarified the analysis data as being associated with the M liquid fractions.

In the Office Action, the Examiner asked how the analysis data from the preceding steps are combined to obtain the n-dimensional image characterized by identifiers and quantifiers and by position. She asks, for example, suppose n=4, m_1=4; m_2=6 m_3=10; m_4=2 and τ=5. Then M is 4*6*10*2=480. Applicant provides the following explanation to assist the Examiner with the example posed above.

A single three dimensional figure may visualize the distribution of one quantifier or one identifier among the fractions of a three dimensional separation. The coordinates x, y, z represent the positions of the resulting fractions (Fig. 2 of the present specification). The amount of the respective quantifier τ is assigned to the color magnitude of the data point by scale.

To display the result of multi-dimensional separation with n>3 and/or more than one characteristic τ as in the given example it is necessary to use multiple images. The given example with n=4 and τ=5 can be displayed in the following way:

Figure 1 displays the separation of the first fraction of m1 yielding the fractions of m2; m3; m4 ; visualized by the coordinated of the colored data point representing τ1.

Figure 2 displays the separation of the second fraction of m1 yielding the fractions of m2; m3; m4 ; visualized by the coordinated of the colored data point representing τ1.

Figure 3 displays the separation of the third fraction of m1 yielding the fractions of m2; m3; m4 ; visualized by the coordinated of the colored data point representing τ1.

Figure 4 displays the separation of the fourth fraction of m1 yielding the fractions of m2; m3; m4 ; visualized by the coordinated of the colored data point representing τ1.

τ2 to τ5 can be displayed in the same manner replacing τ1 by the respective τ. Thus it is possible to display the given example by n x τ= 20 images.

The better choice for analysis of data is a table. For the example given, this table would consist of 4 x 6 x 10 x 2 = 480 rows, the entries of each row showing the respective four-dimensional fraction, the type of identifier and numerical values for quantifiers with that fraction. The following table is showing the given example.

Fractions 1-480	τ_1	τ_2	τ_3	τ_4	τ_5
$m_{1/1}$; $m_{2/1}$; $m_{3/1}$ $m_{4/1}$	Identification 1	6	100	85	0.89
$m_{1/4}$; $m_{2/6}$; $m_{3/10}$ $m_{4/2}$	Identification 1	10	0.34	45	1.008

All table items are random values for given $\tau_{1\text{-}5}$.
The table is especially useful to analyze data by database or spreadsheet calculation and the better choice for n>3 separation dimensions.

The Examiner then asks how is the information from 2400 (τxM) identifications combined to produce the 4-dimensional image of the proteome, particularly when the number of proteins present in the proteome is unknown?

The real number of proteins of a proteome is according to the state of the art a priory unknown. It is dependent on the rate of synthesis and degradation as well as from protein modification and secretion. The useful information of a proteome analysis consists of congruency ad differences between the results of analysis of different proteomes and data from literature and data bases. Thus, the benefits of the results of the given example M x τ = 2400 items are the results of the comparison with other analyzed proteomes or otherwise known data. Protein identifications obtained e.g. peptide mass fingerprint or sequence tag within the examined fractions are valuable information. But as mentioned above, the real number of proteins within the proteome is unknown and thus it is only possible to compare the identified protein number with an estimation of the protein number of the respective proteome. An example could be the analysis of serum of a patient with and without drug treatment followed by comparison of the results. Differences between the results would suggest effects of the drug treatment. The results of analysis, for example, could deliver changes in protein amount, protein pattern, protein modifications, enzyme activities, amount

of non-protein components within serum as cholesterol and identified proteins.

The Examiner further asks how is the number of liquid fractions or required or desirable for each step determined? The required or desirable number of liquid fractions for each step is dependent on:

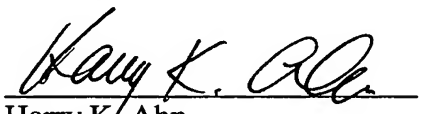
i) the used sample with the number and the characteristics of proteins; and

ii) the character and quality of separation.

As mentioned in point 2, the number of proteins can only be estimated. Protein modifications may change the protein characteristics and may hardly be predicted. Thus it is not possible to arrange the number of fractions a priory according to the sample characteristics. Hence, the person skilled in the art that is performing the separations has to arrange number and volume of fractions experimentally based on preliminary separation, so that preferably all fractions contains protein to avoid empty fractions and that preferably whole peaks are collected in per fraction to achieve the best separation result.

Based upon the above amendments and remarks, Applicant respectfully requests reconsideration of this application and its earlier allowance. Should the Examiner feel that a telephone conference with Applicant's attorney would expedite the prosecution of this application, the Examiner is urged to contact him at the number indicated below.

Respectfully submitted,



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